BACKGROUND:

- The pesticidal effect of OX5034 is species-specific as it only affects the reproductive success of *Ae. aegypti* through mating between OX5034 *Ae. aegypti* males and *Ae. aegypti* females that are already present in the release area.
  - OX5034 GE male *Ae. aegypti* mosquitoes with the tTAV trait are released into the environment to mate with wild female *Ae. aegypti* mosquitoes. (Male mosquitoes do not bite.)
  - All female offspring from matings of GE male mosquitoes with wild female mosquitoes die. Male offspring from matings of GE male mosquitoes with wild female mosquitoes survive, and can pass the lethal tTAV trait to the subsequent generation. Over time, *Ae. aegypti* mosquito populations are reduced in areas where OX5034 mosquitoes are released.
  - OX5034 also contains the marker DsRed2 protein, which turns red under visible light, making the mosquitoes trackable for measuring the effectiveness of the trials.
- In March 2019, EPA received an application for an Experimental Use Permit (EUP) for two years to assess the efficacy of OX5034 *Aedes aegypti* mosquitoes in the United States. The registrant proposed to release the genetically engineered mosquitoes on 6,600 acres in Texas and Florida.
- In April 2020, EPA approved an EUP for this technology to enable field testing to occur during 2020 in Florida and Texas. We understand releases have been limited to Florida and only began in 2021.
- During the comment period for the EUP granted in 2020, the public raised concerns regarding potential allergic reactions from mosquito bites, exposures to novel proteins, and disease transmission by Oxitec GE female mosquitoes. Note, without tetracycline in the environment, such GE female mosquitos will not be present in field trials.
- In March 2021, EPA received an amendment application to extend the EUP in Florida by another 24 months (on up to 6,240 acres/same acreage, new sites) and expand testing to include California (on up 84,600 acres). The EUP amendment would allow generation of additional data in different climatic zones as well as new trial designs for consideration of whether to approve a full FIFRA section 3 registration of OX5034 mosquitoes.
- On August 31, 2021, EPA announced receipt of Oxitec's amendment application in the Federal Register and issued a pesticide announcement with a 30-day opportunity for the public to submit comments on the proposed extension and expansion. 12,961 total comments and 100 unique sets of comments were received. EPA's risk assessment and comment response to the original EUP remain in the docket and are available to the public during this time. Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

- OCSPP (OPP IO and BPPD) have met with Friends of the Earth and the FL Keys Environmental Coalition several times over the last year. In addition, these two groups have submitted multiple letters that BPPD has responded to during that time.
- **Friends of the Earth,** Center for Food Safety, Foundation Earth, FL Keys Environmental Coalition, GMO Free USA, and International Center for Technology Assessment indicated together their intent to sue EPA for violations of the Endangered Species Act for this action by sending a Notice of Intent to Sue (NOI) to Former Administrator Wheeler (received on June 12, 2020). No suit has been filed as of November 2021.

Human Health and Ecological Conclusions from Review of the Initial EUP

- EPA determined that there will be no unreasonable adverse effects for humans or the environment due to introgression of OX5034 background strain genetics into the local *Ae. aegypti* population. EPA evaluated OX5034 mosquitoes for key traits that could increase the ability of mosquitoes to transmit disease, result in larger populations numbers, or result in more robust mosquitoes. EPA collaborated

with the United States Centers for Disease Control and Prevention (CDC) in reviewing data and making this decision.

Human Health Risk Assessment Conclusions from the Initial EUP

- Only male OX5034 mosquitoes are released into the environment. Because male mosquitoes do not feed on humans (they do not bite), they do not pose a human health risk.
- Oxitec's OX5034 female mosquitoes do not survive to become adults without tetracycline. Tetracycline acts as an antidote to the OX5034 female mosquito-lethal trait.
- EPA evaluated human health risk of OX5034 mosquitoes.
  - A determination of the toxicity and allergenicity of the two substances in Oxitec's OX5034 mosquitoes that 1) kill female mosquitoes, tTAV-OX5034, and 2) allow trained personnel to identify OX5034 via fluorescence, DsRed2-OX5034, has not been made.
  - However, because no OX5034 female mosquitoes are being released or are expected to emerge in the environment, exposure is negligible and therefore, so is the potential risk from tTAV-OX5034 and DsRed2-OX5034.

Ecological Risk Assessment Conclusions from the Initial EUP

- EPA evaluated the risk of OX5034 mosquitoes to non-target organisms (bats, amphibians, etc.).
  - No direct adverse effects due to consumption of OX5034 males by non-target organisms is expected based on acute oral toxicity studies and bioinformatics analyses.
  - *Ae. aegypti* mosquitoes (of which OX5034 mosquitoes are) are not a sole or critical food source for non-target organisms, so no indirect adverse effects are expected should there be a decrease in the local mosquito population.
  - After careful consideration of potential direct or indirect interactions that OX5034 Ae. aegypti mosquitoes may have with nontarget organisms (i.e., organisms that are not Ae. aegypti), EPA concluded that no adverse effects are anticipated for any nontarget organisms as a result of the experimental permit to release OX5034 Ae. aegypti mosquitoes based on the screening level assessment that showed no risks of concern at the taxa level. This finding means that there are no discernible effects to nontarget organisms reasonably expected to occur within the action area. As no adverse effects are anticipated for any nontarget organism (i.e., no discernible effects to nontarget organisms are reasonably expected to occur within the action area), which necessarily includes any threatened or endangered species (listed species), EPA therefore reached a "No Effect" determination for direct and indirect effects to listed species, and their critical habitats.

TALKING POINTS:

- The Oxitec mosquitoes have significant potential to advance the protection of public health. EPA will review data on the effectiveness of Oxitec's mosquitoes from the testing under the EUP to determine how well the Oxitec mosquitoes work in reducing the number of *Ae. aegypti* mosquitoes in treated areas.
- Only male OX5034 mosquitoes are released during testing. No genetically modified female OX5034 mosquitoes have been detected during 2021, the first year that releases have occurred under the current EUP.

Ex. 5 Deliberative Process (DP)

- EPA takes its role of protecting the public from insect-borne diseases very seriously.
- EPA carefully considered the original EUP application for a genetically engineered mosquito by Oxitec and is again doing so with the pending EUP amendment application.
- EPA's decision in 2020 was based on the science, specifically, a risk assessment that determined that unreasonable adverse effects risks to human health or the environment are **NOT** expected as a result of the proposed testing under the EUP granted in 2020.

- If approved, the EUP amendment request extending the testing period and adding California test sites would be subject to requirements that are in place for the current EUP. For example,
  - EPA currently requires that Oxitec not release OX5034 mosquitoes near potential environmental sources of tetracyclines, which could impact the OX5034 female mosquito-lethal trait.
  - EPA mandates that Oxitec monitor for OX5034 mosquito female offspring. In the unlikely event Oxitec finds genetically modified female offspring, they are required to immediately cease releases, apply conventional pesticides targeting the adult and larval mosquito stages, and continue monitoring until no female OX5034 mosquitoes are found for two consecutive generations.
  - EPA is currently determining if any changes or additions to these requirements are necessary to address any unique issues related to use in California.